Amendments to the Drawings:

Formal drawings are submitted herewith. Approval by the Examiner is respectfully requested.

Attachment: Replacement Figures 1 and 2

REMARKS

Claims 1-21 and 25-27 are rejected. Claims 22-24 are withdrawn from consideration. Claims 1-27 are subject to restriction and/or election requirement. Claims 1, 15, 25 have been amended. Claim 9 has been canceled. Claims 1-8, 10-27 are presently pending in the application. Favorable reconsideration of the application in view of the following remarks is respectfully requested.

The basis for the amendment of claim 1 is found in original claim 9, as well as pg. 9, lines 15-18 (polymeric matrix), pg. 8, line 1 (reversible), and pg. 9 lines 17, 29, pg. 10, lines 14 and 16 (2-dimensional) of the specification as originally filed. The amendment of claim 15 is based on pg. 9 lines 17, 29, pg. 10, lines 14 and 16 (2-dimensional). The amendment of claim 25 is simply a correction in wording of a Markush group.

Rejection of Claims 1-21 and 25-27 under 35 USC § 112:

The Examiner has rejected Claims 1-21 and 25-27 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, indicating that:

Claim 1 is indefinite or unclear of the spatial relationship of the bead and the medium.

Claim 1 is also unclear if the bead surface and the medium are spatially related.

Claim 15 is missing the "comprising" language.

Claim 25 seems to recite a Markush group, please use appropriate Markush language, i.e. is selected from a group consisting of A, B and C.

Claim 26 is unclear of the spatially relationship of the light stabilizer and the photochromic compound or the medium, or the surface of the bead.

The Applicants have amended claims 15 and 25 accordingly.

With respect to the relationships questioned in claims 1 and 26, the claims, simplified, describe a bead comprising a photochromic compound in a polymeric matrix, the bead having a receptor molecule on its surface. Read literally, the bead is made up of polymer. (See pg. 11, lines 13-27) A photochromic compound is dispersed in the polymer and a receptor molecule is

located on the polymeric-bead surface. Applicants have replaced the term "medium" with the phrase "polymeric matrix" to clarify the composition of the claimed bead.

Rejection of Claims 1-3 and 7-19 Under 35 U.S.C. §102(e):

The Examiner has rejected Claims 1-3 and 7-19 under 35 U.S.C. §102(e) as being anticipated by Leblans et al. (US 2004/0069857), indicating that Leblans teaches a microcarrier such as polystyrene beads loaded or encoded with photochromic compound such as 1,2-Bis(2-mehoxy-5-phenyl-3-thienyl) perfluorocyclopentene, the microcarriers are functionalized with one or more ligands bound to the surface of the microcarriers, and ligands specifically binds to the target analytes.

Leblans relates to a method for the manipulation for an identification purpose of a microcarrier comprising the steps of: (a) an identification purpose step of the microcarrier, and (b) a positioning and orientation step prior to or during the identification purpose step, wherein the identification purpose step is a detection step for the detection of a identifiable or encoded microcarrier and a labeling step resulting in a identifiable or encoded microcarrier. The invention further relates to an apparatus for the manipulation for identification purposes of a microcarrier comprising means for identification purposes such as a microscope or labeling means such as a high spatial resolution light source, and means for the positioning and orientation of the microcarriers and to a microcarrier suitable for use in a method according to the invention.

The present invention relates to color coded beads made up of a reversible photochromic compound, which confers on the bead a distinct optical signature, in a polymeric matrix. The bead has a receptor molecule on its surface, which is capable of binding to a target analyte. The color coded bead is for use in a 2-dimensional microarray for detecting target analytes. The present invention also relates to the color coded beads on a 2-dimensional support.

A claim is anticipated only if each and every element as set forth in the claim is found either expressly or inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. The present claims require a reversible photochromic compound. Leblans [0056] indicates that the photochromic compounds are

irreversible. As a result, the Applicants request the Examiner to reconsider and withdraw the rejection.

Claims 2, 3, and 7-15 benefit from dependence on claim 1, which, as discussed above, Applicants believe is novel with respect to Leblans. Claims 16, 17 and 18, benefit from dependence on claim 15, which, as discussed above, Applicants believe is novel with respect to Leblans.

Rejection Of Claims 20 and 21 Under 35 U.S.C. §103(a):

The Examiner has rejected Claims 20 and 21 under 35 U.S.C. §103(a) as being unpatentable over Leblans, as discussed above, in view of Chee (US 6,429,027), as Chee teaches a two-dimensional array of microspheres randomly immobilized in wells of a substrate, wherein the concentration of the microspheres can range from a single microsphere to 2 billion microspheres per cm2, the microspheres bear biological probes in the form of a bioactive agent, the microspheres comprise a dye in the form of chromophores that can be developed to produce a unique optical signature that allows one to visually identify the microspheres and the bioactive agent bound to the microspheres (see claim 5, col. 21, line 25). Chromophores as defined by Chee absorb light and convert the absorbed light into heat, which is a photo initiated process (see col. 2, lines 8-10).

Since Chee uses wells as substrate for the bead array and Leblans also use wells as a microarray support, it would have been obvious to one of ordinary skills in the art coat the wells of the array in Leblans with 1 single microsphere to 2 billion microspheres per squared cm as taught by Chee. Furthermore, it would have been obvious to one of ordinary skills in the art to coat microcarriers on wells at such ranges since it has been held that where the general conditions of a claim are disclosed in the prior arts, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

Leblans relates to a method for the manipulation for an identification purpose of a microcarrier comprising the steps of: (a) an identification purpose step of the microcarrier, and (b) a positioning and orientation step prior to or during the identification purpose step, wherein the identification purpose step is a detection step for the detection of a identifiable or encoded microcarrier and a labeling step resulting in a identifiable or encoded microcarrier. The invention further relates to an apparatus for the manipulation for

identification purposes of a microcarrier comprising means for identification purposes such as a microscope or labeling means such as a high spatial resolution light source, and means for the positioning and orientation of the microcarriers and to a microcarrier suitable for use in a method according to the invention.

Chee relates to compositions and methods for decoding microsphere array sensors. The invention relates to sensor compositions comprising a composite array of individual arrays, each located at discrete sites, to allow for simultaneous processing of a number of samples. The invention further provides methods of making and using the composite arrays.

The present invention relates to color coded beads made up of a reversible photochromic compound, which confers on the bead a distinct optical signature, in a polymeric matrix. The bead has a receptor molecule on its surface, which is capable of binding to a target analyte. The color coded bead is for use in a 2-dimensional microarray for detecting target analytes. The present invention also relates to the color coded beads on a 2-dimensional support.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the reference or in the general knowledge available to one skilled in the art to modify the reference, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all the claim limitations.

The present invention requires a reversible photochromic compound. Leblans [0056] indicates that the photochromic compounds are irreversible. Chee also fails to mention or suggest a color coded polymeric bead containing a reversible photochromic compound. Therefore, the references fail to provide the necessary motivation.

Chee and Leblans also fail to provide any likelihood of success in utilizing reversible photochromic compounds in microbeads for use in arrays, as neither disclose the use of a color coded polymeric bead containing a reversible photochromic compound. Further, the present invention provides advantages not achieved by Chee and Leblans in the absence of reversible photochromic compounds. For example, the presently claimed color coded beads and arrays are reusable (pg. 7, line 30 – pg. 8, line 2: "*Importantly, since the process with photochromic dyes is completely reversible, analyte-sensor emission detection and color-code generation in microspheres can be repeated.*"). In addition, the

color coded beads and array containing the same can be colored on demand (pg. 7, lines 21-29: "*One advantage is that since the color in microsphere can be generated on demand by using actinic radiation, the present invention allows for interference- or noise-free monitoring (or detection) of fluorescence signal generated from sensor-analyte interaction. Another advantage is that the fluorescence signal intensity generated from the analyte-sensor interaction is not attenuated or quenched.*").

Chee and Leblans also fail to disclose all the limitations of the present claims, as neither Chee nor Leblanc disclose reversible photochromic compounds utilized in polymeric beads for the determination of biological compounds in arrays.

Therefore, since the references, alone and in combination fail to suggest the necessary motivation, fail to provide any likelihood of success, and fail to disclose all of the present claim limitations, the Applicants request that the Examiner reconsider and withdraw the rejection.

Rejection Of Claims 4-6 and 25-27 Under 35 U.S.C. §103(a):

The Examiner has rejected Claims 4-6 and 25-27 under 35 U.S.C. 103(a) as being unpatentable over Leblans, as discussed above, and in view of Knowles (US 5,585,042), as Knowles teaches photochromic naphthopyrans which can be incorporated into polymeric materials such as poly(methyl methacrylate) or polystyrene, teaches mixing stabilizers with photochromic compounds, stabilizers such as hindered amine, and singlet oxygen quenchers to improve the light fatigue resistance of the photochromic substances, teaches that the photochromic naphthopyrans can be incorporated into the polymeric materials or host materials as mixture of photochromic compounds to exhibit a desired resultant color, the amount of photochromic substance or composition should be sufficient to produce a photochromic effect, and compatible dyes can be applied to host along with the photochromic compounds to achieve a more aesthetic result, for medical reasons, making it obvious to one of ordinary skills in the art to load the polymeric microcarriers of Leblans with photochromic compound such as naphthopyrans mixed with stabilizer as taught by Knowles so as to improve light fatigue resistance-of the photochromic substances, as one of ordinary skills in the art would be motivated to combine the two references because both teach that photochromic compounds can be loaded on polymer host or microcarriers,

and, as Leblans also teaches using organic photochromic compound, Knowles teaches an organic photochromic compound of naphthopyran, making it obvious to one of ordinary skills in the art add a mixture of different photochromic compounds or a photochromic compound and a fluorescent dye (non-photochromic compound) with controlled ratio to the microcarriers of Leblans according to the suggestion of Knowles for a more aesthetic result.

Leblans relates to a method for the manipulation for an identification purpose of a microcarrier comprising the steps of: (a) an identification purpose step of the microcarrier, and (b) a positioning and orientation step prior to or during the identification purpose step, wherein the identification purpose step is a detection step for the detection of a identifiable or encoded microcarrier and a labeling step resulting in a identifiable or encoded microcarrier. The invention further relates to an apparatus for the manipulation for identification purposes of a microcarrier comprising means for identification purposes such as a microscope or labeling means such as a high spatial resolution light source, and means for the positioning and orientation of the microcarriers and to a microcarrier suitable for use in a method according to the invention.

Knowles relates to novel reversible photochromic naphthopyran compounds substituted at the number eight carbon atom on the naphtho portion of the naphthopyran ring with, for example, a methoxy group and polymeric organic host materials that contain or that are coated with such compounds. Optically clear articles such as ophthalmic lenses or other plastic transparencies that incorporate the novel naphthopyran compounds or combinations thereof with complementary photochromic compounds, e.g., certain spiro(indoline)type compounds, are also described.

The present invention relates to color coded beads made up of a reversible photochromic compound, which confers on the bead a distinct optical signature, in a polymeric matrix. The bead has a receptor molecule on its surface, which is capable of binding to a target analyte. The color coded bead is for use in a 2-dimensional microarray for detecting target analytes. The present invention also relates to the color coded beads on a 2-dimensional support.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the reference or in the general knowledge available to one skilled in the art to modify the reference, there must be a reasonable

expectation of success, and the prior art reference must teach or suggest all the claim limitations.

The present invention requires a reversible photochromic compound in a polymeric matrix, which produces a color coded bead for use in a microarray for detecting target analytes. Leblans [0056] indicates that the photochromic compounds used in biological arrays are irreversible. Knowles teaches the use of reversible photochromic compounds, however, these compounds are only mentioned for use in sunlight-induced reversible color change (col. 1, lines 22-24: "*Various classes of photochromic compounds have been synthesized and suggested for use in applications in which a sunlight-induced reversible color change or darkening is desired.*"), optical applications (col. 2, lines 17-19: "*In recent years, photochromic plastic materials, particularly plastic materials for optical applications, have been the subject of considerable attention.*"), ophthalmic lenses (col. 2, line 20 "*In particular, photochromic ophthalmic plastic lenses have been investigated because of the weight advantage they offer, vis-a-vis, glass lenses.*"), transportation (col. 2, lines 22-24: "*Moreover, photochromic transparencies for vehicles, such as cars and airplanes have been of interest because of the potential safety features that such transparencies offer.*"), and textiles and coatings ("*coating compositions such as paints, and verification marks on security documents, e.g., documents such as banknotes, passports and drivers' licenses for which authentication or verification of authenticity may be desired.*"). See also col. 5, lines 24-37 ("*Compounds represented by graphic formula I may be used in those applications in which organic photochromic substances may be employed, such as optical lenses, e.g., vision correcting ophthalmic lenses and plano lenses, face shields, goggles, visors, camera lenses, windows, automotive windshields, aircraft and automotive transparencies, e.g., T-roofs, sidelights and backlights, plastic films and sheets, textiles and coatings, e.g., coating compositions such as paints, and verification marks on security documents, e.g., documents such as banknotes, passports and drivers' licenses for which authentication or verification of authenticity may be desired. Naphthopyrans represented by graphic formula I exhibit color changes from colorless to colors ranging from yellow to orange.*"); col. 10, lines 25-29 ("*More preferably, the host material article is a solid transparent or optically clear material, e.g., materials suitable for optical applications, such as plano and*

ophthalmic lenses, windows, automotive transparencies, e.g., windshields, aircraft transparencies, plastic sheeting, polymeric films, etc."); col. 11, lines 22-24 ("*More particularly, contemplated is use of the photochromic naphthopyrans of the present invention with optical organic resin monomers used to produce optically clear polymerizates, i.e., materials suitable for optical applications, such as for example plano and ophthalmic lenses, windows, and automotive transparencies.*"). MPEP 2143.01 III states "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. In re Mills, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)". There is no suggestion in Leblans to use a reversible photochromic compound used in optical transparency applications for microcarrier identification. There is no suggestion in Knowles to use an irreversible photochromic compound used in microcarrier identification in optical transparency applications of Knowles. MPEP 2143.01 IV states "A statement that modifications of the prior art to meet the claimed invention would have been " 'well within the ordinary skill of the art at the time the claimed invention was made' " because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a prima facie case of obviousness without some objective reason to combine the teachings of the references. Ex parte Levengood, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). See also In re Kotzab, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000)" Knowles and Leblans are not in the same field of the art, as Leblans deals with assays for the identification of biological compounds, and Knowles deals with optical transparency applications, such as vision correcting ophthalmic lenses and plano lenses, face shields, goggles, visors, camera lenses, windows, automotive windshields, aircraft and automotive transparencies, T-roofs, sidelights and backlights, plastic films and sheets, textiles and coatings, coating compositions such as paints, and verification marks on security documents, documents such as banknotes, passports and drivers' licenses. MPEP 2143.01 I. states "There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." In re Rouffet, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998)" "The test for an implicit showing is what the combined teachings, knowledge of one of

ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." In re Kotzab, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). See also In re Lee, 277 F.3d 1338, 1342-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002) (discussing the importance of relying on objective evidence and making specific factual findings with respect to the motivation to combine references); In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). As discussed above, Knowles and Leblans do not suggest the use of a color coded bead comprising a reversible photochromic compound in a polymeric matrix, for use in a microarray for detecting target analytes and Knowles and Leblans are not in the same field of art. In addition, Knowles and Leblans do not relate to the same problem. Leblans deals with the problems specific to the labeling and tracking of biological compounds in a complex system to enable identification. Knowles, as cited by the Examiner, deals with improvements in aesthetics, and light fatigue resistance-of the photochromic substances of sun-light induced, reversible color changing or darkening compounds used in optical applications. Finally, MPEP 1243.01 V. states "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Knowles, col. 1, lines 10-20 state "The present invention relates to certain novel naphthopyran compounds. More particularly, this invention relates to novel photochromic naphthopyran compounds with unexpected properties, and to compositions and articles containing such novel naphthopyran compounds. When exposed to light radiation involving ultraviolet (UV) rays, such as the ultraviolet radiation in sunlight or the light of a mercury lamp, many photochromic compounds exhibit a reversible change in color. When the ultraviolet radiation is discontinued, the photochromic compound will return to its original color or colorless state." The use of an irreversible photochromic compound as taught by Leblans would render the invention of Knowles unsatisfactory for its intended purpose, as any color or shade change would only occur once.

Knowles and Leblans also fail to provide any likelihood of success in utilizing reversible photochromic compounds in microbeads for use in arrays,

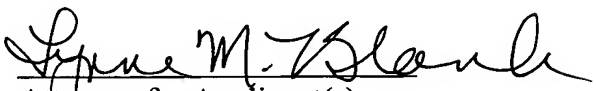
as neither disclose the use of a color coded polymeric bead containing a reversible photochromic compound. Further, the present invention provides advantages not achieved by Knowles and Leblans in the absence of reversible photochromic compounds. For example, the presently claimed color coded beads and arrays are reusable. In addition, the color coded beads and array containing the same can be colored on demand. MPEP 2145 D3 states that "The totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. In re Hedges, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986). Leblans teaches the use of irreversible photochromic compounds. Substituting reversible photochromic compounds, as taught for different applications not related to the field of art of Leblans, would be proceeding contrary to accepted wisdom in the art of Leblans.

Knowles and Leblans also fail to disclose all the limitations of the present claims, as neither Knowles nor Leblanc disclose reversible photochromic compounds utilized in polymeric beads for the determination of biological compounds in arrays.

Therefore, since the references, alone and in combination fail to suggest the necessary motivation, fail to provide any likelihood of success, and fail to disclose all of the present claim limitations, the Applicants request that the Examiner reconsider and withdraw the rejection.

It is believed that the foregoing is a complete response to the Office Action and that the claims are in condition for allowance. Favorable reconsideration and early passage to issue is therefore earnestly solicited.

Respectfully submitted,



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Copies of Formal Drawings

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